

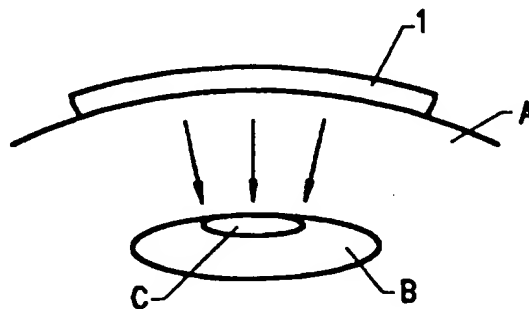
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## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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<b>(21) International Application Number:</b> PCT/US96/18747 <b>(22) International Filing Date:</b> 22 November 1996 (22.11.96) <b>(30) Priority Data:</b> 7/306162 24 November 1995 (24.11.95) JP <b>(71) Applicant (for all designated States except US):</b> EKOS CORPORATION [US/US]; 234 Alverson Boulevard, Everett, WA 98201 (US). <b>(72) Inventors; and</b> <b>(75) Inventors/Applicants (for US only):</b> TACHIBANA, Katsuro [JP/JP]; 1-6-18, Kusagae, Cho-ku, Fukuoka 810 (JP). TACHIBANA, Shunro [JP/JP]; 1-6-18, Kusagae, Cho-ku, Fukuoka 810 (JP). <b>(74) Agent:</b> DAVIS, Paul; Wilson, Sonsini, Goodrich & Rosati, 650 Page Mill Road, Palo Alto, CA 94304-1050 (US).	<b>(81) Designated States:</b> AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>	

**(54) Title:** HEMOSTASIS MATERIAL AND APPARATUS**(57) Abstract**

A method and apparatus for creating hemostasis includes introducing a cavitation threshold reducing agent to the body. Ultrasound energy is applied at a selected site in the body at a frequency sufficient to create hemostasis.



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HEMOSTASIS MATERIAL AND APPARATUS  
BACKGROUND OF THE INVENTION

Field of the Invention

5           This invention relates generally to hemostasis, and more particularly to a method and apparatus to cause hemostasis using ultrasound and ultrasound sensitive drugs.

Description of Related Art

10           In the case of death by car accidents, gastric ulcers, ruptures of esophageal varices, massive bleeding is a frequent cause of death. Particularly in emergency situations, It is important to stop bleeding as quickly as possible. To increase the rate of survival, it is essential to stop the bleeding as s quickly as possible.

15           In auto accidents, strong mechanical forces frequently cause damage to internal organs in the abdomen. This is a major cause of death. When endoscopic fibers or catheters cannot be used for treatment of rupture of organs or intra-liver bleeding, it is difficult to stop bleeding without surgical intervention. This is why it is difficult to effectively stop the bleeding at the  
20           accident site before transfer to a hospital.

            With bleeding from gastric ulcers or esophageal varices rupture, there are several methods of endoscopy to stop bleeding. However, this is not 100% effective. The current treatment used for hemostasis is laser or high radio  
25           frequency energy to burn the origin of the bleeding. However, the success rate is not that high. Current treatment methods can cause damage to locations other than the at the site of bleeding.

            Another method of treatment is the use of drugs as thrombin which chemically induce reactions and cause coagulation. In one method, the drug is sprayed to the bleeding site and coagulation reaction is activated. However, this  
30           is not completely effective to stop all bleeding.

### BRIEF DESCRIPTION OF THE FIGURES

Figure 1 is a diagram illustrating the treatment of bleeding when it is difficult to use catheters or endoscopes.

5 Figure 2 is an illustration of an ultrasound therapy generator useful with the present invention.

Figure 3 illustrates hemostasis treatment with the use of a catheter or endoscope.

Figure 4 is a cross section view of the tip of the endoscope of Figure 3.

10

### SUMMARY

An object of the invention is to provide a method and apparatus to provide hemostasis without the need for major surgical intervention.

Another object of the invention is to provide a method and apparatus for enhancing phonophoresis.

15

A further object of the invention is to provide a method and apparatus for enhancing phonophoresis with the introduction of a threshold reducing agent to the body.

20 Still another object of the invention is to provide a method and apparatus to create hemostasis by introducing a cavitation threshold reducing rate and applying ultrasound energy.

These and other objects of the invention are achieved in a method for enhancing phonophoresis. A cavitation threshold reducing agent is introduced into the body. Ultrasound energy is applied at a selected site in the body at a frequency sufficient to produce a therapeutic effect.

25

In one embodiment, a method for creating hemostasis includes introducing a cavitation threshold reducing agent to the body. Ultrasound energy is applied at a selected site in the body at a frequency sufficient to create hemostasis.

30 In another embodiment of the invention, an apparatus for creating hemostasis includes a cavitation threshold lowering agent means. Ultrasound energy means are coupled to the cavitation threshold lowering agent means. A

sufficient ultrasound energy wavelength is generated to create hemostasis at a selected site in the body.

In one embodiment the cavitation threshold lowering agent is Rose Bengal or a hematoporphryn.

5

#### DETAILED DESCRIPTION

The present provides a method for enhancing phonophoresis. A cavitation threshold reducing agent is introduced to the body. Ultrasound energy is applied at a selected site in the body at a frequency sufficient to produce a therapeutic effect. A method is also provided for creating hemostasis with the introduction of the cavitation threshold reducing agent and the application of ultrasound energy.

The present invention also is an apparatus for creating hemostasis. The apparatus includes a cavitation threshold lowering agent means and an ultrasound energy means that is coupled to the cavitation lowering agent means. An ultrasound energy wavelength is produced that is sufficient to create hemostasis at the selected site in the body. An apparatus for creating hemostasis includes a hemostasis agent means. The apparatus also includes an ultrasound energy means which generates an ultrasound frequency that creates hemostasis at the selected site in the body.

Any number of cavitation threshold reducing drugs or hemostasis drugs can be used. Suitable drugs include but are not limited to Rose Bengal, hematoporphryns, and the like. In one embodiment the amount of delivered ultrasound energy can be in the range of 0.1 to 1000 Watts per square centimeter.

After intravenous injection of the ultrasound sensitive drug and delivery of the drug to the bleeding site, the site of the bleeding is exposed to ultrasound from an ultrasound device. This results in activation of the ultrasound sensitive drug and coagulation of the blood. In this way, hemostasis is achieved quickly and efficiently.

30

The methods and apparatus of the invention provide a hemostasis material that effectively and rapidly stop bleeding effectively without performing major surgical intervention such as large scale operations.

5 The methods and apparatus of the invention are used to treated a variety of different bleeding sites including but not limited to bleeding by organ rupture hemorrhage within the liver, and the like.

Referring now to Figure 1, there are times when it is difficult to use catheters or endoscopes to stop bleeding from organs. An ultrasound sensitive drug is first intravenously injected into the patient. An ultrasound diagnostic  
10 device is used (not shown in the diagram) to patient A. After locating and confirming the bleeding site C in organ B, ultrasound therapy is performed with the ultrasound therapeutic device 1 by concentrating ultrasound energy at bleeding site C for the purpose of coagulating the blood at the site of the damaged organ, vessel and the like..

15 Referring now to Figure 2, a suitable therapeutic ultrasound device 1 is shown. In one embodiment, ultrasound device 1 can include multiple ultrasound elements 1b which are attached to an interior side of a main body portion 1a of ultrasound device 1. An ultrasound vibration element 1b can be a plate type ultrasound element which has an electrode on both sides. By loading the  
20 electrode with ultrasound frequency electrical signals, ultrasound is emitted in the direction of the arrows.

Ultrasound therapy device 1 is bendable according to the shape of the patient A's body. This permits ultrasound energy to be concentrated to the bleeding site C.

25 Diagram 3 illustrates a method of therapy where it is possible to use the catheter or endoscopy for stopping bleeding from the organs including but not limited to gastric ulcers, esophageal varices, and the like.

Figure 4 shows the cross section view of the structure of an endoscope 2 useful with the present invention. In the method of treatment, the ultrasound  
30 sensitive drug is first intravenously injected to the patient. Then an esophageal or gastric endoscope 2 is introduced at bleeding site C in organ B including but not limited to the stomach as shown in Figure 3. Locally or in a large area,

hemostasis is performed by exposing ultrasound from ultrasound vibrating element 2c. In one embodiment, ultrasound vibrating element 2c is attached to the tip of the endoscope 2, sheath 2a. The ultrasound sensitive drug in the blood is then activated by ultrasound. This produces instant coagulation which is a more effective hemostasis method than conventional methods.

In one embodiment, an ultrasound vibrating element 2c is a cylinder piezo electric element in which an optical fiber 2b passes through the center and the electrode is placed on the outer and inner side. The electrode receives electrical signals of ultrasound frequencies which induce ultrasound energy in the direction of the arrows. When ultrasound vibrating elements 2c are shaped in a cylinder, ultrasound energy is emitted evenly toward the radius of the axis of endoscope 2. However, the shape of ultrasound vibrating element 2c is not limited to illustrated geometry. In other embodiments, a disk-like ultrasound vibrating element 1b is positioned where optical fiber 2b passes through the center at the tip of the sheath 2a of the endoscope 2. In embodiment, ultrasound is concentrated at the axis of endoscope 2.

The methods and apparatus of the present invention provide treatment of bleeding by injecting one or more ultrasound sensitive drugs to the patient along with exposure to ultrasound energy. The methods and apparatus of the present invention are particularly useful immediately after bleeding has begun. This permits treatment and stoppage of bleeding can be stopped while the patient is transferred in an ambulance. This decreases the mortality rate of massive bleeding. Death rates from trauma are lowered by temporarily stopping the bleeding. Thereafter, major surgical intervention can be performed at the hospital. Death rates from bleeding are then reduced. The methods and apparatus of the present invention are effective for very severe bleeding which is difficult to treat with conventional surgical methods. Additionally, because ultrasound energy can be exposed to a large area, multiple bleeding sites of different origins can be treated at the same time.

Ultrasound energy can be exposed exterior to a patient's body for hemostasis. Deep locations of the body including but not limited to the liver, abdominal aorta, other organs bleeding and the like, are treated without surgical

intervention. Because ultrasound energy is used, body organs and structure are not damaged. This is in contrast with and will be safely used compared with laser or high radio frequency therapies where body organs and structures can be suffer damage when energy from these sources is applied to the body.

5           The foregoing description of a preferred embodiment of the invention has been presented for purposes of illustration and description. It is not intended to be exhaustive or to limit the invention to the precise forms disclosed. Obviously, many modifications and variations will be apparent to practitioners skilled in this art. It is intended that the scope of the invention be defined by the following  
10           claims and their equivalents.

          What is claimed is:



CLAIMS

1. A method for enhancing phonophoresis comprising:  
introducing a cavitation threshold reducing agent to a body; and  
5 applying ultrasound energy at a selected site in the body at a frequency  
sufficient to produce a therapeutic effect.
2. The method of claim 1, wherein the cavitation threshold reducing agent is  
Rose Bengal.  
10
3. The method of claim 1, wherein the cavitation threshold reducing agent is  
hematoporphryn.
4. A method for creating hemostasis comprising:  
15 introducing a cavitation threshold reducing agent to a body; and  
applying ultrasound energy at a selected site in the body at a frequency  
sufficient to create hemostasis.
5. The method of claim 4, wherein the cavitation threshold reducing agent is  
20 Rose Bengal.
6. The method of claim 4, wherein the cavitation threshold reducing agent is  
hematoporphryn.
- 25 7. An apparatus for creating hemostasis comprising:  
a cavitation threshold lowering agent means; and  
ultrasound energy means coupled to the cavitation threshold lowering  
agent means and generating an ultrasound energy wavelength sufficient to create  
hemostasis at a selected site in a body.  
30
8. The apparatus of claim 7, wherein the threshold lowering agent is Rose  
Bengal.

9. The apparatus of claim 7, wherein the threshold reducing agent is hematoporphryn.
10. An apparatus for creating hemostasis comprising:  
5 a hemostasis agent means; and  
ultrasound energy means generating an ultrasound frequency that creates hemostasis at a selected site in a body.
11. The apparatus of claim 10, wherein the threshold lowering agent is Rose  
10 Bengal.
12. The apparatus of claim 10, wherein the threshold reducing agent is hematoporphryn.

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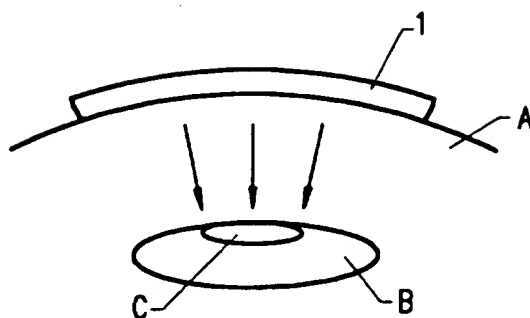


FIG. 1

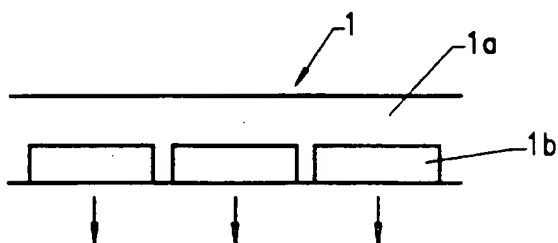


FIG. 2

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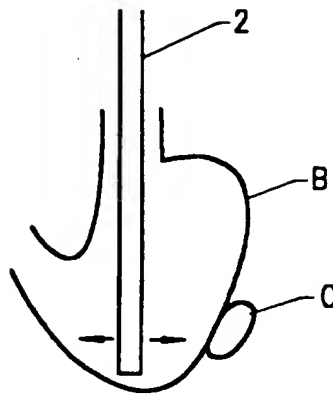


FIG. 3

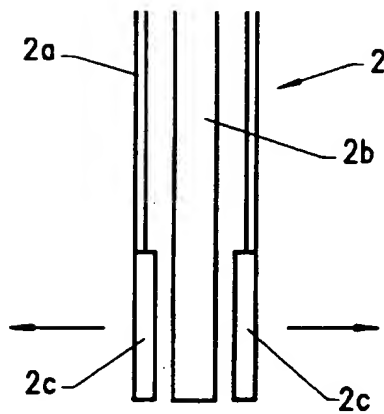


FIG. 4

# INTERNATIONAL SEARCH REPORT

Intern. Application No  
PCT/US 96/18747

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 6 A61M37/00 A61N7/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 6 A61M A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 971 991 A (UMEMURA KOHSHIRO ET AL) 20 November 1990 see column 2, line 13 - line 53 ---	7-12
X	DE 39 19 592 A (OLYMPUS) 22 February 1990  see column 6, line 33 - line 49 see claims 1,14,15; figure 1 ---	7,9,10, 12
X	EP 0 351 610 A (HITACHI LTD) 24 January 1990 see abstract see page 5, line 28 - line 30 ---	7,9,10, 12
X	WO 94 06355 A (CORAJE) 31 March 1994 see page 7, line 16 - line 33 see page 11, line 19 - line 34; figure 1 --- -/--	7,10

☒ Further documents are listed in the continuation of box C.

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Date of the actual completion of the international search

3 April 1997

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C(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 226 740 A (DORNIER) 1 July 1987 see page 2, line 4 - line 8 see page 2, line 25 - page 3, line 6; figures 1,2 ---	7,10
A	US 5 053 006 A (WATSON) 1 October 1991  see abstract ---	7,8,10, 11
A	DE 40 20 596 A (TACHIBANA) 2 January 1992 see abstract; figure 1 ---	7,10
A	GB 2 167 305 A (VERNON SMITH) 29 May 1986 see abstract; figure 2 -----	7,10

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 96/18747

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 1-6  
because they relate to subject matter not required to be searched by this Authority, namely:  
PCT Rule 39.1(iv) Method for treatment of the human or animal body by  
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2. ☐ Claims Nos.:  
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an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all  
searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment  
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3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report  
covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is  
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Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 96/18747

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